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10/692,684

10/27/2003

Tetsuya Suga

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11/29/2010

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EXAMINER

BROOKS, KRISTIE LATRICE

ART UNIT

PAPER NUMBER

1616

NOTIFICATION DATE

DELIVERY MODE

11/29/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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|------------------------------|--------------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/692,684 | Applicant(s) SUGA ET AL. | |
| | Examiner KRISTIE L. BROOKS | Art Unit 1616 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 12-17, 19-36, 38-46, 48-53 and 75-78 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 12-17, 19-36, 38-46, 48-53, and 75-78, is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>9/27/10</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 27, 2010 has been entered.

Status of Application

2. Claims 1,12-17, 19-36, 38-46, 48-53, and 75-78 are pending.
3. Receipt and consideration of Applicants amendments/remarks filed on September 27, 2010 is acknowledged.
4. Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to

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be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1,12-17, 19-36, 38-46, 48-53, and 75-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uchiyama et al. (US 2002/0119164) in view of Kropf et al. (US 6,858,214) and Desai et al., Gastrointestinal Uptake of biodegradable microparticles: Effect of particle size, Pharmaceutical Research, Volume 13. No. 12, 1996.

Applicant claims a composition comprising superfine particles of a β -glucan derived from a water extract of a mushroom, wherein the superfine particles have an average particle diameter of 10 μ m or less, as determined in the form of a dispersion in water.

Applicant also claims a process for producing superfine particles comprising superfine pulverizing a β -glucan derived from a water extract of a mushroom.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Uchiyama et al. teach *Agaricus blazei* (a mushroom) in whole, particulate, or extracted form, can be used to treat forms of damage to the skin caused by toxins and chemicals (see the abstract and page 2 paragraph 25)). *Agaricus blazei* (a mushroom) in whole, particulate, or extracted form, when taken internally, also offers protection against various disorders including autoimmune disorders (see the abstract and page 2 paragraph 26). The identified compounds that have been extracted from *Agaricus blazei* and that are of particular use in the invention include beta glucans (see page 3 paragraph 34 and claims 1 and 12).

The extraction may be done by immersing the mushroom in particulate form, in an aqueous solution or parts thereof with The extraction can also be done by immersing particulate *Agaricus blazei*, in plain hot water, preferably over 90°C (see page 2 paragraph 32 and page 3 paragraph 33). The extract may be freeze dried or concentrated using water or methanol/acetone solutions (see page 3 paragraph 33). The ratio of mushroom to water is preferably between 1:2 and 1:100 (see page 3 paragraph 33). The concentration of the extract is preferably between 0.05% and 50% v/v (see page 3 paragraph 44).

The extract can be used with other active or inactive ingredients and can be formulated as a liquid, capsule, pill, tablet, solution suspension or emulsion (see page 4 paragraphs 45 and 51). The extract can be formulated as a solution by dissolving the *Agaricus blazei* extract in water, oils, propylene glycol, etc. (see

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page 4 paragraphs 45 and 51). A wide variety of agents may be added to produce better dispersions or to accentuate cooling, soothing, or protective properties.

The extract is useful for treating skin disorders and internal diseases such as autoimmune diseases topical or internally (orally) (see page 3 paragraphs 37-43 and page 4 paragraphs 48-49). The extract may treat diabetes, lupus, certain types of cancer and can be used in the form of a food, drink or dietary product (see page 4 paragraph 50).

**Ascertainment of the difference between the prior art and the claims
(MPEP 2141.02)**

Uchiyama et al. teach the *Agaricus blazei* extract (i.e. beta glucans) can be present in particulate form but do not teach the particle size of the extract. Uchiyama et al. also do not teach lecithin. These deficiencies are cured by the teachings of Kropf et al. and Desai et al.

Kropf et al. disclose the use of nanoscalar water-soluble β -glucans. The β -glucans are contained in cosmetic and/or pharmaceutical preparation having particle diameters in the range of 10 to 300 nm (equivalent to 0.01 to 0.30 μ m) (see column 1, lines 43- 47). The composition can further contain adjuvants known in the cosmetic and/or pharmaceutical industry (see column 3, lines 19-34). Column 5, lines 51-52 teach that lecithin can be used in the composition as a hyperfating agent.

Desai et al. teach the effect of particle size on the gastrointestinal uptake of biodegradable microparticles. In general, the efficacy of uptake of 100nm size microparticles by the intestinal tissue (e.g. Peyer's patch) was 15-250 folds higher when compared to large size microparticles. This is particularly important in the design of oral drug delivery systems (see the abstract).

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

One of ordinary skill in the art would have been motivated to formulate the *Agaricus blazei* extract (i.e. beta glucans) with the instant particle size (i.e. 10µm or less) because the instantly claimed beta glucans are known for use topically to treat skin conditions and orally in pharmaceutical formulations. It is well known in the art to formulate beta glucans with the instantly claimed particle size for cosmetic or dermatological purposes, as suggested by Kropf et al. Further, it is known in the art that using a smaller particle size (e.g. 100nm) can increase the efficacy and delivery of the active to the intestinal tissue, as suggested by Desai.

Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to formulate the *Agaricus blazei* extract (i.e. beta glucans) with the instant particle size (i.e. 10µm or less) because it is an obvious particle size that beta glucans can be prepared when used for pharmaceutical or cosmetic purposes. And further, because it will result in

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enhanced uptake of active, resulting in improved bioavailability and enhanced drug absorption, and reduced toxicity.

Although Uchiyama et al. do not teach lecithin can be used in the formulations, it is a common and known hyperfating agent (emulsifier) that can be used in formulations containing beta-glucan, as suggested by Kropf et al. Thus, it would have been obvious for one of ordinary skill in the art to incorporate lecithin into the formulation taught by Uchiyama et al., because it is a common additive to add to formulations depending on the desired form of the final product.

With respect to claims 39 and 44, although Uchiyama et al. do not specifically teach the step of filtering the extract, it would have been obvious to one of ordinary skill in the art to filter the extract, so as to remove any excess solution, impurities or additional materials that are not needed in the extract.

With respect to claims 16-17, it is also noted that the reference does not teach that the product can be made by the process instantly claimed, i.e. filtering, filtering and then concentrating and/or cooling. However, the patentability of a product does not depend on its method of production. If the product in the product-by-process claims is the same or obvious from a product in the prior art, the claim will be held unpatentable even if the prior product is made by a different process (See MPEP 2113).

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as

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evidenced by the reference, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed September 27, 2010 have been fully considered but they are not persuasive.

Applicant's argues that the primary reference Uchiyama et al., is overly generic and does not actually disclose or suggest that the water extract of mushroom *Agaricus blazei* contains any β -glucans.

This argument is not persuasive. Uchiyama et al. specifically teaches that extracts of *Agaricus blazei* can be prepared using "water extraction" or preferably "hot water extraction" (see paragraphs 32 and 33). Identified compounds in the extracts include beta-glucans (see paragraph 34). Thus, it would have been obvious to one of ordinary skill in the art to try water extraction or hot water extraction to obtain beta glucans since they are preferred methods in obtaining the extracts of identified compounds (i.e. beta glucans).

Applicants argue that Kropf et al. teach the particle size of a yeast extract of beta- glucans and not mushroom extracts of beta-glucans, and thus is related to a different invention. Applicant argues that beta glucans extracted from yeast are structurally different. Applicant has provided references to establish that beta glucans derived from yeast are structurally different from beta glucans extracted from mushrooms.

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Applicant's argument is not convincing. Uchiyama et al. already teach that the mushroom extract of *Agaricus blazei* can be present in particulate form. Although Kropf et al. teach that the beta glucans are prepared from a yeast extract, the end result is the same. In both references, the beta glucans are being used for the same purpose and in the same type of formulations. It would have been obvious to one of ordinary skill in the art to try to prepare the beta glucans taught in Uchiyama et al. within the same particle size range as instantly claimed (i.e. less than 10 microns) because it has been disclosed by Kropf et al. that beta glucans can be used effectively in cosmetic and pharmaceutical formulations when prepared within the instantly claimed particle size range (i.e. less than 10 microns). Furthermore, it is known in the art that a smaller particle size (e.g. 100 nm) has a higher efficiency of uptake when compared to larger particle sizes, as suggested by Desai. The particulate carrier system is important for oral drug delivery in order to enhance absorption and bioavailability.

Therefore, Applicant's evidence of unexpectedness is not persuasive and the rejection is maintained.

Conclusion

6. No claims are allowed.
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIE L. BROOKS whose telephone number is (571)272-9072. The examiner can normally be reached on M-F 8:30am-6:00pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Kristie L Brooks

Examiner, Art Unit 1616

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616